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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,669	12/21/2001	Rama Akella	SBI-111	1708

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EXAMINER

RUSSEL, JEFFREY E

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 02/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/027,669

Applicant(s)

AKELLA ET AL.

Examiner

Jeffrey E. Russel

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 14, 15, 20-29 and 32-36 is/are allowed.
- 6) ☒ Claim(s) 1-12, 16-18, 30 and 31 is/are rejected.
- 7) ☒ Claim(s) 13 and 19 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

1. In view of the new grounds of rejection set forth below, the finality of the previous Office action is withdrawn. The amendment after final rejection filed January 20, 2004 has been entered. Claims 1-36 are pending in this application.

2. Claims 13 and 19 are objected to because of the following informalities: At claim 13, line 3, it is believed that "TGF- μ 2" should be changed to "TGF- β 2". At claim 19, line 2, "patent's" should be changed to "patient's". Appropriate correction is required.

3. The effective filing date of instant claims 1-31 is deemed to be December 21, 2001, the filing date of the instant application. Instant claims 1-31 and 33 are not deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of parent application 09/748,038 because the parent application, under the test of 35 U.S.C. 112, first paragraph, does not disclose the genus of TGF- β superfamily polypeptides; does not disclose vinyl pyrrolidone polymers in general; does not disclose the molecular weight range of about 2.5 kD to about 20 kD; does not disclose water or aqueous buffer solutions as solvents for the growth factor composition; does not disclose the polymer concentration range of about 0.1% w/v to about 70% w/v or the narrower ranges of instant claims 8-10; does not disclose the viscosity ranges recited in instant claims 26-29; does not disclose promoting soft tissue regeneration in general; and does not disclose increasing the bioavailability of growth factors.

The effective filing date of instant claims 32-34 and 36 is deemed to be October 16, 1998, the filing date of grandparent application 09/173,989. These claims are deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of the '989 application because the '989 application, under the test of 35 U.S.C. 112, first paragraph, discloses the claimed invention.

The effective filing date of instant claim 35 is deemed to be December 22, 2000, the filing date of parent application 09/748,038. Claim 35 is not deemed to be entitled under 35 U.S.C. 120 to the benefit of the filing date of grandparent application 09/173,989 because the '989 application, under the test of 35 U.S.C. 112, first paragraph, does not disclose a bone-derived growth factor mixture wherein about 60% of the protein content is histones, ribosomes, and growth factors.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claim 31 is rejected under 35 U.S.C. 102(b) as being anticipated by the Chinese Patent 1,163,780. The Chinese Patent '780 teaches forming an aqueous solution of bone morphogenetic protein and combining it with a second aqueous solution of bFGF and PVP. The resultant composition is used for osteogenesis stimulation, i.e. is used to generate cartilage and bone tissue. The bFGF in the composition stimulates capillary formation inside cartilage, which is a major step in the formation of bone by bone induction. The PVP acts to solubilize both the bone morphogenetic protein and the bFGF so that a complete suspension can be prepared. In in vivo testing, the composition is administered by injection. See, e.g., page 2; page 4, lines 10-12; page 8, lines 13-23; and page 11, lines 7-13; of the translation. The cartilage whose growth is stimulated by the composition of the Chinese Patent '780 is a soft tissue.

5. Claims 1-12, 16-18, and 30 are rejected under 35 U.S.C. 103(a) as being obvious over the Chinese Patent 1,163,780. The Chinese Patent '780 teaches forming an aqueous solution of bone morphogenetic protein and combining it with a second aqueous solution of bFGF and PVP. The resultant composition is used for osteogenesis stimulation, i.e. is used to generate cartilage and

Art Unit: 1654

bone tissue. The bFGF in the composition stimulates capillary formation inside cartilage, which is a major step in the formation of bone by bone induction. The PVP acts to solubilize both the bone morphogenetic protein and the bFGF so that a complete suspension can be prepared. In in vivo testing, the composition is administered by injection. See, e.g., page 2; page 4, lines 10-12; page 8, lines 13-23; and page 11, lines 7-13; of the translation. The cartilage whose growth is stimulated by the composition of the Chinese Patent '780 is a soft tissue. Because the composition of the Chinese Patent '780 comprises bFGF which stimulates capillary formation, the composition is capable of promoting angiogenesis. The Chinese Patent '780 does not teach a molecular weight or solution concentration for its PVP. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine a molecular weight and solution concentration for the PVP of the Chinese Patent '780 because molecular weight and solution concentration are art-recognized result-effective variables which are routinely determined and optimized in the polymer, solution chemistry, and pharmaceutical arts.

6. Claims 1-12, 16-18, and 30 are rejected under 35 U.S.C. 103(a) as being obvious over the Chinese Patent 1,163,780 as applied against claims 1-12, 16-18, and 30 above, and further in view of the Robinson et al text (Reference C8 of the Information Disclosure Statement filed October 22, 2003). As noted above, although the Chinese Patent '780 does not teach a molecular weight for its PVP, the Robinson et al text teaches that typical molecular weights for injectable human preparations are 12, 15, 17, and 30 kDa. See page 10, last paragraph. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine a molecular weight for the PVP of the Chinese Patent '780 from within the range of molecular weights taught by the Robinson et al text because molecular weight is an art-

Art Unit: 1654

recognized result-effective variable which is routinely determined and optimized in the pharmaceutical arts as shown by the Robinson et al text.

7. Applicant's arguments filed January 20, 2004 have been fully considered but they are not persuasive.

The amendment to the claims filed January 20, 2004 overcomes the claim objections and the rejection under 35 U.S.C. 112, first paragraph, set forth in paragraphs 1 and 2 of the Office action mailed November 19, 2003.

The rejection over the Mueller et al article (Swiss Med. Wkly., Vol. 131, pages 23-25) set forth in paragraph 5 of the previous Office action is withdrawn in view of the declarations by May and by Akella, filed January 20, 2004, which show that subject matter of the Mueller et al article relied upon by the examiner in the rejection was derived from the instant inventors. Accordingly, the Mueller et al article is not "by another" and the Mueller et al article is not available as prior art under 35 U.S.C. 102(a).

Certain of Applicants' claims are now rejected over the Chinese Patent 1,163,780, upon which Chemical Abstract 132:40522x was based. Further, the examiner now also relies in part upon the Robinson et al text (Reference C8 of the Information Disclosure Statement filed October 22, 2003). Although no date is given for this reference in the IDS, the examiner has supplied a copy of Dyer (U.S. Patent Application Publication 2002/0025340), which shows in [0099] that the Robinson et al text was published in 1990.

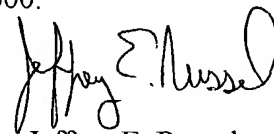
8. Claims 14, 15, 20-29, and 32-36 are allowed. Claim 13 would be allowable if rewritten or amended to overcome the claim objection set forth in this Office action. Claim 19 would be allowable if rewritten to overcome the claim objection set forth in this Office action and to

Art Unit: 1654

include all of the limitations of the base claim and any intervening claims. With respect to instant claim 13, the BMP of the Chinese Patent '780 does not inherently contain at least two of the growth factors as required by the claim, and there is no motivation to include at least two of the specified growth factors in the composition of the Chinese Patent '780. With respect to instant claim 14, the Chinese Patent '780 does not teach or provide any motivation to include one of the growth factors recited at claim 14, line 4, in its composition. With respect to instant claim 15, the Chinese Patent '780 does not teach or provide any motivation to include each of the growth factors recited at claim 15, line 3, in its composition. With respect to instant claims 19-29 and 32-36, because the Chinese Patent '780 teaches the use of its compositions to stimulate bone growth, there is no motivation to administer the compositions to a patient's heart, to administer the compositions subcutaneously or intramuscularly or intravenously, or to administer the compositions to ischemic tissue.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (571) 272-0961. The fax number for formal communications to be entered into the record is (703) 872-9306; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel
Primary Patent Examiner
Art Unit 1654

JRussel
February 23, 2004